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EXAMINER	
MCGILLEM, LAURA L	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 12/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No. 10/806,346	Applicant(s) URTHALER ET AL.	
	Examiner Laura McGillem	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *25-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-24) in the reply filed on 10/30/2006 is acknowledged. The traversal is on the ground(s) that the claims of Group I and Group II are related in that the reactor of the claims of Group II (claims 25-39) is used to carry out the method of the claims of Group I. Applicants submit that a search concerning the patentability of the invention of one group is likely to uncover art of interest to the other group. Applicants submit that the Examiner must examine all the claims if the search and examination of the claims can be made without serious burden, even if Applicants' claims encompass multiple independent and distinct inventions. MPEP, 8th Ed. (August 2006), § 803, at page 800-4, left-hand column, lines 1-16. Applicants submit that the search of Groups I and II would not impose any burden upon the Examiner, because a search concerning the patentability of the invention of one group is likely to uncover art of interest to the other group. This is not found persuasive because the method of Group I does not require the reactor of Group II. A search for the method of Group I would not encompass the limitations of the reactor of Group II and would therefore constitute a burdensome search.

The requirement is still deemed proper and is therefore made FINAL.

Claims 25-39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/30/2006. Claims 1-24 are under examination.

Specification

The use of the trademarks TWEEN®, TRITON® (paragraph 0028) and QIAGEN® has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The disclosure is objected to because of the following informalities: the spelling of the words “Endotoxine” and “Quiagen” in paragraph 0040 appear to be typographical errors. It would be remedial to correct them to “Endotoxin” and “QIAGEN”.

Appropriate correction is required.

Claim Objections

Claim 8 is objected to because of the following informalities: the word “appliying” appears to be misspelled and should be corrected to “applying”. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because it recites the phrase "gently flow downward" and the metes and bounds of "gently" are not clear. It is not clear if gentle flow refers to the speed of flow, and if so, what flow speed would meet the limitation of gently flowing? It is not clear whether the phrase "gently flow downward" refers to the angle at which the lysate would be flowing downward, and if so, what downward angle would meet the limitation of gentle downward flow?

Claim 1 is vague and indefinite because it recites the phrase "reactor that is partially filled, in its lower part" and the metes and bounds of partially filled are not clear. For example, it is not clear if the reactor is partially filled (i.e. filled only in the lower part) or the lower part of the reactor is only partially filled.

Claim 7 is vague and indefinite because it recites the phrase "the process". There is insufficient antecedent basis for this limitation in the claim. It is not clear what process Applicants intend to be accelerated by the increasing pressure. It is not clear if the Applicants intend to accelerate the method to produce a biomolecule of interest or accelerate separation of the lysate form the precipitate (step d).

Claims 10-11 are vague and indefinite because they recite the phrase "gently mixing" and "gently mixed", respectively, and the metes and bounds of "gently" are not clear. The skilled artisan would not know what mixing rate would constitute gentle mixing in order to meet the limitation of the claims.

Claim 16 is vague and indefinite because it recites the phrase "transportation between step b) and step d)" and it is not clear to what place the combined solution is being transported. Specifically, steps b), c) and d) are method steps (i.e. an activity or process). According to the Merriam-Webster online dictionary, the word transport means to convey from one place to another. As the claim is written, it is not clear how a solution will be conveyed from the action of disintegrating to the action of separating. It might be remedial to amend the claim to recite "precipitating <u>after step b) and before step d)</u> ~~during transportation between step b) and step d)~~".

Claim 22 is vague and indefinite because it recites the phrase "connecting the two or more individual steps" and it is not clear what is being connected. Claim 23 is vague and indefinite because it recites the phrase "step a) is operated in a continuous mode by being connected to step b)" and it is not clear what is being connected. As discussed above, method steps describe an activity or process. The Merriam-Webster online dictionary defines connect as "to become joined" and "to join or fasten together usually by something intervening". As the claim 22 is written, it is not clear how the activity steps from b) to e) (disintegrating, precipitating, separating, purifying) will be physically joined to one another. As the claim 23 is written, it is not clear how the activity step a) (cultivating) will be connected to step b) (disintegrating).

Claim 24 recites the limitation "the cell mass". There is insufficient antecedent basis for this limitation in the claim. Claim 24 is dependent on claim 1, which does not recite a "cell mass". Step a) of claim 1 comprises cultivating host cells and optionally

harvesting and resuspending the cells and it is not clear which of these steps would produce the intended cell mass.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 5, 7-9, 15, 17 and 19-20 are rejected under 35 U.S.C. 102(b) as being anticipated by The QIAGEN Transfection Source Book, 1999, pages 15 and 48-55 (herein, QIAGEN).

QIAGEN teaches a method to purify plasmid DNA from bacterial cultures. QIAGEN teaches the step of growing liquid cultures of bacteria comprising plasmids in selective LB medium for 12-16 hours at 37°C with shaking, followed by harvest by centrifugation of the culture and resuspension in a solution known as Buffer P1 (see steps 1-4 on page 49 and page 55, for example), which reads on cultivating host cells to produce a biomolecule of interest, harvesting and resuspending the cells. QIAGEN teaches that a solution known as Buffer P2 comprising NaOH and SDS is added to the resuspended cell solution to produce a cell lysate (see page 49 step 5, and page 55), which reads on disintegrating the cells by alkaline lysis. QIAGEN teaches that a solution known as Buffer P3, which contains potassium acetate at pH 5.5, is added to the lysate and causes the formation of a fluffy precipitate that comprises genomic DNA, protein,

cell debris and SDS (see page 49 step 6 and page 55, in particular), which reads on precipitating the cell debris and impurities by neutralizing the lysate.

QIAGEN teaches that the mixture of lysate and precipitate is poured into an upright cartridge filter (e.g. clarification reactor) and air pressure is exerted from a plunger without extreme force in order to flow the lysate through a filter. QIAGEN teaches that the lysate is recovered after the filtration (see page 49, steps 7-8, for example), which reads on separation of the lysate from a precipitate. Absent evidence to the contrary and a clear definition of the limitation of gentle downward flow, the step of inserting a plunger without extreme force to push the lysate through the filter meets the limitation of allowing the mixture comprising the precipitate and the lysate to gently flow downward through a clarification reactor to retain the precipitate on top of and within the layer of retention material and wherein the cleared lysate leaves the reactor through the bottom. The insertion of the plunger into the clarification reactor would apply pressurized air in order to apply increasing pressure to the top of the lysate and precipitate mixture to thereby accelerate the process and ensure a constant outflow of the lysate from the filter, and therefore would meet the limitation of claims 7-8. QIAGEN illustrates a Qiafilter that appears to contain retention material in the lower part of the filter device (page 15), which meets the limitation of a clarification reactor partially filled in the lower part with retention material. Absent evidence to the contrary and a specific definition of the limitation of rigid, the Qiafilter is composed of a rigid retention material and meets the limitation of claim 5.

QIAGEN further teaches that the filtered lysate is allowed to contact a positively charged anion-exchange resin by gravity flow so that the plasmid DNA in the lysate binds to the resin (see page 50 step 11 and 13, for example), which reads on a lysate that contains the biomolecule of interest and meets the limitation of claim 2. QIAGEN teaches that plasmid DNA is eluted from the resin with a buffer known as Buffer QN and then precipitated from solution with isopropanol (see page 50, steps 11-14, for example), which reads on a step of purifying the biomolecule of interest such as a plasmid DNA as claimed in claims 19-20. Therefore the method taught by Qiagen meets the limitation of the method of claim 1.

QIAGEN further teaches that the DNA on the resin is washed with Buffer QC to remove contaminants from the plasmid preparation (see page 560, step 11-12, for example) which reads on a washing step between the step of separating the lysate from the precipitate and purifying the plasmid of interest and meets the limitation of claim 9.

Instant claim 15 includes the limitation of a continuous mode step to mix the neutralizing solution with the lysed cell solution. QIAGEN teaches that the Buffer P3 (neutralizing solution) is added to the lysate solution by 4-6 gentle inversions of the tube before adding the mix to the Qiafilter cartridge (clarification reactor). Absent evidence to the contrary, the lysed cell solution and the neutralizing solution would begin mixing when the neutralizing solution was added to the lysate, further mix during the inversions and would continue to mix during incubation in the Qiafilter cartridge until separation therefore meeting the limitation of mixing in a continuous mode.

QIAGEN teaches that a buffer known as QBT buffer that comprises NaCl, MOPS at pH 7.0 and isopropanol is added to the QIAGEN tip containing the anion exchange resin in order to equilibrate the resin and allowed to flow out of the resin until the liquid meniscus reaches the frit above the resin (see page 50 step 10, for example). Absent evidence to the contrary, the lysate comprising the plasmid DNA would mix with the QBT buffer on addition to the column and alter the some parameters of the lysate solution, such as salt composition, pH or conductivity and would therefore meet the limitation of a conditioning step as in claim 17.

Claims 1-5, 9, 15 and 19-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Gonzales (U.S. Patent No. 5,783,686, 7/21/1998).

Gonzales teaches a method to isolate and purify nucleic acids such as plasmid DNA from bacterial cells or yeast lysates (see column 1, lines 16-30 and column 4, lines 22-35, for example). Gonzales teach that bacterial cell cultures are aerobically grown, pelleted by centrifugation and resuspended in a Tris Buffer solution (see column 7, lines 18-35, for example and page 55, for example), which reads on cultivating host cells to produce a biomolecule of interest, harvesting and resuspending the cells.

Gonzales teaches that a solution comprising NaOH and SDS is added to the resuspended cell solution to produce a cell lysate (see column 7, lines 36-39 and 44-46, for example), which reads on disintegrating the cells by alkaline lysis. Gonzales teaches that a solution that contains potassium acetate at pH 5, is added to the lysate to neutralize the mixture and causes the formation of a gummy mass that comprises

chromosomal DNA and protein SDS complexes (see column 7, lines 48-52, in particular), which reads on precipitating the cell debris and impurities by neutralizing the lysate.

Gonzales teaches that the mixture of lysate and gummy mass is filtered in a well of a filter plate (e.g. clarification reactor) using a vacuum pressure to pull the cleared lysate through the filter to the well of a 96-well tissue culture plate, which retains the gummy mass (see column 7, lines 53-57, for example), which reads on separation of the lysate from a precipitate. Absent evidence to the contrary, the disclosed filter plate meets the limitation of a clarification reactor partially filled in the lower part with retention material (Loprodyne/Loprosorb filter) because the upper part of the filter plate would necessarily have some volume to contain the mixture and the gummy precipitate. Absent evidence to the contrary and a specific definition of the limitation of rigid, the filter plate is composed of a rigid retention material and meets the limitation of claim 5.

Gonzales further teaches that silica slurry is added to the filtered lysate and allowed to incubate before another filtration through a filter plate, which retains the silica material (see column 7, lines 58-67, for example), and reads on a lysate that contains the biomolecule of interest and meets the limitation of claim 2. Gonzales teaches that DNA is recovered from the silica by elution with water (see column 8, lines 12-18, for example), which reads on a step of purifying the biomolecule of interest such as a plasmid DNA from the lysate as claimed in claims 19-20. Therefore the method taught by Gonzales meets the limitation of the method of claim 1.

Gonzales discloses a method in which glass beads are treated with hydrophilic material that would selectively binds proteinaceous material and not DNA. Gonzales discloses that DNA can be isolated by allowing DNA and protein containing mixtures to contact hydrophilic glass beads, and subsequently removing the beads to leave behind DNA in solution (see column 2, lines 9-16, for example), which reads on a clarification reactor with a retention material comprised of particulate material in the form of glass beads and meets the limitations of claims 3-4.

Gonzales teaches that the DNA on the silica is washed at least twice with an alcohol solution to remove unwanted material and impurities (see column 3, lines 1-3, column 6, lines 9-25 and column 8, lines 1-12, for example) which reads on a washing step between the step of separating the lysate from the precipitate to purify the plasmid of interest and meets the limitation of claim 9.

Gonzales teaches that the neutralizing solution is added to the lysate solution and reanneals the plasmid DNA. Absent evidence to the contrary, the lysed cell solution and the neutralizing solution would begin mixing when the neutralizing solution was added to the well, and would continue to mix during incubation in the well until separation, therefore meeting the limitation of mixing in a continuous mode in as claimed in instant claim 15.

Gonzales teaches that the method of plasmid DNA purification can be performed using a Biomek automated laboratory workstation (see column 7, lines 26-30 and 41-44, in particular), which reads on a method to purify plasmid DNA wherein at least one step

is operated in an automated mode, absent evidence to the contrary the method would be in a continuous mode.

Claims 1-2, 5-6, 9, 15 and 17-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Marquet et al (WO 95/21250, 8/10/1995).

Marquet et al teach a method for producing plasmid DNA. Marquet et al teach that plasmid DNA containing host bacterial cells are cultured, recovered and resuspended in buffer (see page 8, lines 11-21, and page 20, lines 10-35,for example), which reads on a step of cultivating host cells to produce a biomolecule of interest, harvesting and resuspending the cells. Marquet et al teach that the host cell cells are lysed by alkaline hydrolysis, and the lysate produced is subsequently acidified to facilitate removal of insoluble material (see page 8, lines 22-35 bridging to page 9, lines 1-6, for example), which reads on disintegrating the cells by alkaline lysis and precipitating the cell debris and impurities by neutralizing the lysate. Marquet et al teach that cell debris and impurities can be removed from the lysate containing DNA by filtration through a material that is porous enough for plasmid DNA to pass through, but not insoluble material. Marquet et al teach that the filter device can be comprised of a porous fritted glass disks. Marquet et al disclose that the filtration can be performed using gravity, pressure or vacuum (see page 9, lines 8-30, in particular), which reads on a step of separating the precipitate from the lysate by allowing the mixture to gently flow downward using gravity through a clarification reactor that is partially filled in its lower part with a rigid retention material where the precipitate is retained on top of and within

the retention material and the lysate would flow through the bottom of the reactor. The skilled artisan would know that a gravity filtration device, such as a Buchner funnel (i.e. a clarification reactor) has the retention material or filter in the lower part of the funnel (see page 23, lines 14-20, for example). Marquet et al teach that the plasmid DNA is purified from impurities using size exclusion chromatography (see page 13, lines 10-35, for example). Therefore, the method taught by Marquet et al to purify DNA from a bacterial lysate meets the limitation of claims 1-2.

Marquet et al teach that the filter can be non-flexible, porous fritted glass disks (see page 9, lines 26-28, for example), which meets the limitations of claims 5-6 of a rigid retention material or sinter plates as disclosed in the instant specification paragraph 0113. Marquet et al teach further step to precipitate and collect partially purified DNA using alcohol or PEG precipitation followed by filtration (see page 9, lines 30-35 and page 10, for example), which reads on a wash step before the purification step as in claim 9.

Marquet et al teach that the neutralizing solution is added to the lysate solution. Absent evidence to the contrary, the lysed cell solution and the neutralizing solution would begin mixing when the neutralizing solution was added, and would continue to mix during incubation until separation by filtration, therefore meeting the limitation of mixing in a continuous mode in as claimed in instant claim 15. Marquet et al teach that washed precipitated plasmid DNA is resuspended in GRAS buffer or TE to alter pH and ionic strength (see page 9, lines 1-5, page 12, lines 27-30, page 20, lines 25-27 and page 21, lines 21-15, for example), which reads on a conditioning step and

concentration step, wherein the concentration step takes place before the conditioning step as claimed in claims 17-18.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over The QIAGEN Transfection Source Book, 1999, pages 15, 48-55 (QIAGEN) in view of Craig (U.S. Patent No. 6,381,967, 5/7/2002).

Applicants claim a method to purify a biomolecule of interest wherein a cell mass obtained by cultivating host cells to produce the biomolecule are cryo-pelleted.

The teachings of QIAGEN are outlined in the above rejection. QIAGEN also teaches an optional method step in which the bacterial cells that have been harvested by centrifugation of the culture can be frozen in pellets for later use. QIAGEN does not teach cryo-pelleting as disclosed in the specification as forming cryo-pellets by dropping the liquid material to be frozen into fluid gases and continuously bringing the resulting pellets out of the system.

Craig teaches problems that cause cell death during cell freezing, including death due to formation of large sharp ice crystals that injure the cells, and also cell poisoning due to osmotic dehydration by formation of ice crystals. Craig teaches that freezing can

involve a process of vitrification, which is the solidification of solutions at low temperature without ice crystal formation. Craig teaches that the higher the speed of the temperature change, the lower the viscosity required to vitrify and faster freezing rates lead to smaller ice crystals (see column 1, lines 16-44, for example). Craig teaches that the goal of any cryopreservation process is to minimize cell damage (see column 2, lines 1-30, for example). Craig teaches a freezing method in which a liquid sample is transformed into small drops that are directly contacted with a partially solidified refrigerant. Craig teaches that this method is useful for substances that are susceptible to ice crystal or osmotic damage such as cells, plant material, tissue culture cells, sperm and embryos (see column 3, lines 20-25, column 4, lines 29-40, and column 12, lines 9-20, see, for example).

It would have been obvious to the skilled artisan at the time the invention was made to use the rapid freezing method as taught by Craig to form bacterial cell cryo-pellets for storage prior to a method of biomolecule purification as taught by QIAGEN because QIAGEN suggests that the harvested bacterial cells can be frozen before use and Craig teaches an advantageous method of freezing cells. The motivation to freeze the bacterial cells by dropping them into partially solidified gas to form a cryopellet is the expected benefit of freezing the cells quickly in order to avoid formation of damaging and cytotoxic ice crystals as taught by Craig. There is a reasonable expectation of success to cryopellet bacterial cells before use since this has worked previously as taught by Craig. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said

ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 1 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gonzales (U.S. Patent No. 5,783,686, 7/21/1998) in view of Craig (U.S. Patent No. 6,381,967, 5/7/2002).

Applicants claim a method to purify a biomolecule of interest wherein a cell mass obtained by cultivating host cells to produce the biomolecule are cryopelleted.

The teachings of Gonzales are outlined in the above rejection. Gonzales also teaches an optional method step in which the bacterial cells that have been harvested by centrifugation of the culture can be frozen in pellets for later use. Gonzales does not teach cryo-pelleting as disclosed in the specification as forming cryo-pellets by dropping the liquid material to be frozen into fluid gases and continuously bringing the resulting pellets out of the system.

Craig teaches problems that cause cell death during cell freezing, including cell death due to formation of large, sharp ice crystals that injure the cells, and also cell poisoning due to osmotic dehydration by formation of ice crystals. Craig teaches that freezing can involve a process of vitrification, which is the solidification of solutions at low temperature without ice crystal formation. Craig teaches that the higher the speed of the temperature change, the lower the viscosity required to vitrify cells, and faster freezing rates lead to smaller ice crystals (see column 1, lines 16-44, for example). Craig teaches that the goal of any cryopreservation process is to minimize cell damage

(see column 2, lines 1-30, for example). Craig teaches a freezing method in which a liquid sample is transformed into small drops that are directly contacted with a partially solidified refrigerant. Craig teaches that this method is useful for substances that are susceptible to ice crystal or osmotic damage such as cells, plant material, tissue culture cells, sperm and embryos (see column 3, lines 20-25, column 4, lines 29-40, and column 12, lines 9-20, see, for example).

It would have been obvious to the skilled artisan at the time the invention was made to use the rapid freezing method as taught by Craig to form bacterial cell cryo-pellets to store cells prior to a method of biomolecule purification as taught by QIAGEN because Gonzales teaches that the harvested bacterial cells can be frozen before use and Craig teaches an advantageous method of freezing the cells. The motivation to freeze the bacterial cells by dropping them into partially solidified gas to form a cryopellet is the expected benefit of freezing the cells quickly in order to avoid formation of damaging and cytotoxic ice crystals as taught by Craig. There is a reasonable expectation of success to cryopellet bacterial cells before use since this has worked previously as taught by Craig. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 1 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marquet et al (WO 95/21250, 8/10/1995) in view of Craig (U.S. Patent No. 6,381,967, 5/7/2002).

Applicants claim a method to purify a biomolecule of interest wherein a cell mass obtained by cultivating host cells to produce the biomolecule are cryo-pelleted.

The teachings of Marquet et al are outlined in the above rejection. Marquet et al also teaches an optional step in which the bacterial cells that have been harvested by centrifugation of the culture can be frozen and stored for later use. Marquet et al does not teach cryo-pelleting as disclosed in the specification as forming cryo-pellets by dropping the liquid material to be frozen into fluid gases and continuously bringing the resulting pellets out of the system.

The teachings of Craig are outlined in the above rejections.

It would have been obvious to the skilled artisan at the time the invention was made to use the rapid freezing method as taught by Craig to form bacterial cell cryo-pellets to store cells prior to a method of biomolecule purification as taught by QIAGEN because Marquet et al teach that the harvested bacterial cells can be frozen before processing and Craig teaches an advantageous method of freezing the cells. The motivation to freeze the bacterial cells by dropping them into partially solidified gas to form a cryo-pellet is the expected benefit of freezing the cells quickly in order to avoid formation of damaging and cytotoxic ice crystals as taught by Craig. There is a reasonable expectation of success to cryo-pellet bacterial cells before use since this has worked previously as taught by Craig. Given the teachings of the prior art and the

level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura McGillem whose telephone number is (571) 272-8783. The examiner can normally be reached on M-F 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Laura McGillem, PhD
11/21/2006

DANIEL M. SULLIVAN
PATENT EXAMINER